Dissertation On

Comprehensive Study on Prognosis of Malignant Tumours of Larynx – A Prospective Study

Submitted for
M.S. Degree Examination
Branch IV Oto-Rhino Laryngology

Upgraded Institute of Oto-Rhino Laryngology
Madras Medical College
Chennai – 600 003.

THE TAMIL NADU
Dr.M.G.R. MEDICAL UNIVERSITY
CHENNAI

March 2007

CERTIFICATE

This is to certify that DR. **V. SARAVANAN** is a Post Graduate student during the academic session 2004 to 2007 in Upgraded Institute of Otorhinolaryngology, Government General Hospital ,Madras Medical College,CHENNAI – 600 003

The following dissertation titled "**Comprehensive Study on Prognosis of Malignant Tumours of Larynx – A Prospective Study"** is a bonafide work done by him during the study period and is being submitted to The Tamilnadu Dr.M.G.R.Medical University in partial fulfillment of M.S.(ENT) examination march 2007

DEAN
Madras Medical College &
Govt. General Hospital
Chennai- 600 003

Prof.**S.Ammamuthu**, M.S., D.L.O.,
Professor & Director
Upgraded Institute of Otorhino Laryngology,
Govt. General Hospital
Chennai- 600 003

ACKNOWLEDGEMENT

I express my sincere thanks to **Prof. KALAVATHY PONNIRAIVAN .M.D., Dean** Madras Medical College for permitting me to do this study .

I express my sincere gratitude to **Prof. Dr. S. AMMAMUTHU, M.S.,D.L.O.** Director UIORL for his permission ,subsequent support and encouragement in conducting this study .

I profoundly thank ***Prof.Dr. U. VENKATESAN, M.S., D.L.O.,*** *for his support and encouragement in completing this study*

I profoundly thank Prof**. Dr. A.K. SUKUMARAN, M.S., D.L.O.,** for his support and encouragement in completing this study

I profoundly thank Prof. **Dr. BALU DAVID, M.D., D.M.R.T.,** Prof of Radio therapy for giving me the relevant details in regard to the study

I would be failing in my duty if I do not acknowledge the support and guidance of my Assistant professors who were always ready to clarify my doubts

I thank the cooperation and help provided by my colleague post graduate and all staff members of Upgraded Institute of Otorhinolaryngology who have helped me complete this study

DECLARATION

I, ***DR. V. SARAVANAN,*** solemnly declare that dissertation titled **"Comprehensive Study on Prognosis of Malignant Tumours of Larynx – A Prospective Study"** is a bonafide work done by me at UIORL Madras Medical College, Chennai. under the guidance and supervision of my unit chief **Prof. S. AMMAMUTHU,M.S., D.L.O.,**

This dissertation is submitted to Tamilnadu DR. M.G.R Medical University, towards partial fulfillment of requirement for the award of ***M.S. Degree (Branch – IV) in Otorhinolaryngology.***

Place : Chennai.

Date :

(Dr. V. SARAVANAN)

INTRODUCTION

More than 100 cases of laryngeal malignancy is being detected each year in upgraded institute of otorhinolaryngology Department, Madras Medical College Chennai. So the burden cases of carcinoma of larynx is ever increasing.

Madras Metropolitan tumour registry, a population based cancer registry in chennai states that as of 2002, carcinoma larynx finds a place in top 10 cancers in men. Cumulative risk of getting ca larynx in their life time (0-74) is 1 in 208 and 1in 2000 in male and female respectively. ca larynx affects both sex with male preponderance which affects essential functions of larynx like speech and respiration and causes death.

It is Mandatory to evaluate about the prognostic factors and treatment modalities is of prime importance. Predicting the favourable prognostic factors and choosing correct line of management is of paramount importance to increase the survival rate.

In the era of organ preservation not all cases are subjected to surgery. So radiotherapy is the preferred treatment for most cases. But Radiotherapy carries the risk of residual or recurrent growth. This Dissertation analysis the prognostic factors and treatment modality adopted for 50 cases of our institute since 2004 and their survival rate after 2yrs.

AIM OF THE STUDY

The present study on malignant lesions of larynx is undertaken to study

- The distribution of laryngeal malignancy by age, sex and staging on presentation and known risk factors.
- The different histopathological types and differentiation
- Various treatment modalities adopted
- Assessment of prognostic factors
- Assessment of treatment outcome after 2 yrs.

Review of Literature

Historical Review

- **Ullmann** (1923) demonstrated the presence of viral particles by injecting cell free extracts from papillomatous tissue.

- **Jackobasson** (1976), in his studies in Karolinska Institute in Stockholm, devised score system of grading the malignant potential of tumous.

- **Batsakis** (1979) showed strong association between carcinoma of larynx and cigaratte and pipe tobacco smoking.

- **Crissman** (1979) used the term keratosis, because excess keratin formation is a common feature of the changes observed in laryngeal malignancy. He divided it into three groups according to its severity as keratosis, low grade dysplasia & high grade dysplasia.

- **Bukley** et al (1982) identified three grades of morphological (histological) abnormalities as laryngeal intra epithelial neoplasia (LIN). The changes of LIN are considered to be a morphological manifestation of a neoplastic process, not a precancerous lesion.

- **Manguso and Hanfo** (1982) have done extensive study of the larynx by using computerized tomography in benign tumours and laryngeal trauma. In cases of tumour extension, CT has made in possible to detect, Spread to anterior commisssure, Deep extension to paraglottic, para anytenoid areas, pre epiglottic spaces, Cartilage invasion, Extension of pyriform fossa tumours.

- **Neuman and Byers** (1982) in this study in otorhinolaryngology recorded the peak incidence of age was between fifth and sixth decade for laryngeal carcinoma.

- **Rothman** (1982) described cancer epidemiology and prevention of laryngeal tumours.

- **Ogura** et al (1983) showed the laryngeal carcinoma patients are always heavy smokers and incidence of metastases is 5 - 10%. Thirty fold risk of developing larygeal squamous cell carcinoma for men smoking atleast a pack and a half of cigarettes per day for more than Ten years.

- **Cummings** et al (1996) showed the factors involving the malignant tumours of larynx and hypopharynx. He also reported that all of the patients develop squamous cell carcinoma were documented as reflux into laryngo pharynx.

- **Singh** et at (1996) described the basaloid-squamous carcinoma a distinct histological entity. It is a variant of squamous cell carcinoma and it is preferentially located in the larynx especially in supraglottic sites. Recurrence rate is higher than the control group. These indicates post operative irradiation should be taken into consideration.

- **Reddy** et al (1997) showed 75% to 95% of cure rate in small laryngeal cancers depending on thesite, tumour bulk, and degree of infiltration.

- **Me Caffrey** et all (1998) described verrucous carcinoma of larynx - a variant of squamous cell carcinoma. most patients are men aged twenty nine to eighty with a peak incidence between fifty and sixty nine years and very high proportion to smokers.

- **Yilmaz** et al (1998) has described the prognostic factors that include, sex, age, pathologic features of tumour. The most important adverse factors for laryngeal cancers include increasing T stage and M stage.

- **Laccourreye** (1999) has done conservative modality of treatment in patients with stage I-II squamous cell carcinoma of glottis.

APPLIED ANATOMY OF LARYNX

Alterations in the functions of larynx have a significant impact not only on the respiratory physiology but also on that of deglutition.

Anatomically the larynx consists of3 regions - supraglottis, glottis and subglottis. Each region is anatomically and embryologically distinct with separate lymphatic channels. Cancer of each region is therefore different in terms of its presentation, growth patterns, spread, treatment and prognosis.

Supraglottis: The sites included in the supraglottic region are the epiglottis, the aryegpiglottic folds and the arytenoids. Inferiorly lie the false cords and the ventricle which separate the supraglottis from the glottis. Ths suprglottis has a rich lymphatic network. Lymphatics from this region exit through the thyrohyoid membrane along with the superior larygeal vessels into the jugulodigastric lymph nodes. Spread occurs early in this region.

Glottis: The glottis consists of the rihght and the left vocal cords uniting anteriorly to form the anterior commissure. The vocal cord is membranous in its anterior two-thirds consist of vocalis muscle and its overlying epithelium. The posterior one-third is cartilaginous, made up of vocal process of the arytenoid. The glottis extends inferiorly for a distance of 5mm where it is continuous with the subglottis. Glottis extends between superior and inferior arcuate lines. At the line of junction, the squamous epithelium changes to columnar epithelium. The lymphatics of the true vocal cord are sparse. Lymphatics from the glottis and subglottis pass through the circothyroid

ligament and drain into the prelaryngeal (Delphian) nodes, paratracheal nodes and the deep cervical nodes along the inferior thyroid artery.

Subglottis: This consists of a mobile part from below the true vocal cords to the upper border of the cricoid cartilage (mucosa covering conus elasticus) and a fixed part which extends upto the inferior border of the cricoid.

Reinke's Space: This is a submucosal space between the mucosa of the glottis and the underlying vocalis muscle. It acts as a bursa allowing the mucosa to slide over the underlying tissues producing fluency in normal speech. The mucosa of the vocal cord can therefore be stripped of without causing damage to the underlying soft tissues with practically no alteration in the quality of voice.

Pre-epiglottic Space of Boyer : This is a fat-filled space lying between the hyoid bone and thyrohyoid membrane anteriorly and the infrahyoid epiglottis posteriorly, hyoepiglottic ligament superiorly. Tumour invasion of this space signifies adanced disease and is staged as T3 in the TNM classification. The space is rich in lymphatics and relatively radioresistant because of the sparse blood supply. The space is continuous on either side, with the paraglottic space deep to the quadrangular membrane.

Paraglottic Space of Tucker: The paraglottic space is a paired space between the conus elasticus and quadrangular membrane medially and the thyroid cartilage laterally. The paraglottic space contains the thyro-arytenoid muscle. Infiltration of this space causes fixity of the vocal cord by involvement of this muscle. Inferolaterally this space is continous with the gap between the thyroid and cricoid cartilage permitting the tumour an easy exit route to extralaryngeal spread.

Blood Supply:

Larynx above the vocal folds is supplied by superior laryngeal artery a branch of superior thyroid artery. The superior laryngeal veins drain drain into the superior thyroid veins.

Below the vocal cords by the inferior laryngeal artery a branch of inferior thyroid artery. Inferior laryngeal vein drain into the inferior thyroid vein.

Nerve Supply:

The innervation of the larynx is through vagus by superior and recurrent laryngeal nerves. All intrinsic muscles of larynx are innervated by the recurrent laryngeal nerve except for cricothyroid which is innervated by external laryngeal nerve.

Sensory by internal laryngeal nerve innervating mucous membrane up to the level of vocal cords. The recurrent laryngeal nerve supplies it below the level of the vocal cords.

Lymphatic Drainage:

The lymphatics of the larynx are separated by the vocal folds into an upper and lower group. The part of the larynx above the vocal folds is drained by vessels which accompany the superior laryngeal vein, pierce the thyrohyoid membrane and empty into the upper deep cervical lymph nodes: whereas the zone below the vocal folds drains, together with the inferior vein, into the lower part of the deep cervical chain often through the prelaryngeal and pretracheal nodes. The vocal folds are firmly bound down to the underlying vocal ligaments and this results in an absence of lymph vessels, a fact which accounts for the clearly defined watershed between the upper and lower zones.

Supraglottis drains through vessels which accompany the superior laryngeal pedicle through the thyrohyoid membrane to reach the upper deep cervical nodes.

The lower system drains directly into the deep cervical nodes through vessels which pass through or behind the cricothyroid membrane or drain into the prelaryngeal, pre tracheal or paratracheal nodes before reaching the deep cervical nodes.

Nodal levels as followed at Memorial Sloan-Kettering Hospital

Level I : Submental and submandibular groups

Level II : Upper jugular group

Level III: Middle jugular group

Level IV : Lower jugular group

Level V: Posterior triangle group

Level VI: Anterior compartment group (visceral group) parathyroid, pretracheal, prelaryngeal etc.

Lever VII : These are nodes of the upper anterior mediastinum

AETIOLOGY OF LARYNGEAL MALIGNANACY:

No single factor has been decisively proven to produce laryngeal carcinoma in man. Smoking and excessive alcohol intake are frequently encountered in patients with laryngeal and hypopharyngeal carcinomas. Some studies have implicated some racial predilection, urban dwellers, radiation exposure, asbestos, laryngeal kerotosis and leukoplakia, air pollution, Unidentified social and possibly genetic factors, and uncommon occupational influences, as a predisposing factors, but convincing proof is lacking". Second Primary is Possible because of common etiology

a. **Smoking**: Smoking is a strong risk factor for the development of laryngeal cancer. In two separate studies it was found that 96.5% and 97.2% respectively of patients with laryngeal Cancer were smokers. Men smoking at least a pack-and-a-half cigarettes per day for more than 10 years have a relative 30 fold risk of developing laryngeal Carcinoma. The risk of cancer from tobacco usage appears to be strongest for current smokers, and it declines markedly when smoking is stopped

b. **Tobacco Chewing**: Tobacco has long been implicated as an important etiological agent in the development of larynx malignanacy.

c. **Alcohol (Ethanol)**: Many studies shows that consumption of all types of alcohol considered an another important risk factor. The relative risk of alcohol drinkers (compared with non drinkers) develop laryngeal carcinoma was increased 2.2 fold. Another source of alcohol that has been associated with Aero-digestive squamous cell carcinoma is available as mouth washes, the ethanol content of

which may range upto 28%. The dose related increase in risk of laryngeal squamous cell carcinoma in alcohol is almost equivalent to smoking.

d. **Occupation**: The development of laryngeal cancer related to occupational factors appears to relatively uncommon and not well documented, as compared with other work related to head and neck cancer. All labourers expect agriculture and semiskilled workers (such as factory workers) were in greater risk than professionals. Exposure to asbestos, wood dust and cement dust, isopropyl alcohol, leather working, metal processing, mustard gas, nickel / nickel refining, sulfuric acid/other acids, textiles fibres/processing, coal and tar products have reported in some studies.

e. **Diet and Vitamin Deficiency**: Diet and vitamin deficiency also attributed especially vitamin A deficiency and Vitamin C and protease inhibitors. A study evaluating the effect of cruciferous vegetable (such as cabbage and broccoli) containing insoles and flavinoids, which are known to inhibit the development of chemically induced cancer, showed that a high intake of these vegetables decrease the risk of laryngeal carcinoma.

f. **Irradiation Exposure** : The relationship between irradiation and the subsequent development of squamous cell carcinoma has been strongly suspected. The development of laryngeal cancer following irradiation for thyrotoxicosis and has been reported. Ex smokers are more prone to this type of lesions, possibly reflecting the importance of other carcinogenic risk factors.

g. **Viral Factors**: The Human Papilloma Virus (HPV) is recognized as an etiological factor in laryngeal cancer. Usually all the patients developing squamous cell carcinoma were cigarette smokers and reflux into laryngopharynx. Smith studied relationship between Human Papilloma Virus and laryngeal cancer. Human Papilloma Virus type found laryngeal include subtypes 6,11,16,18,30 and 33, Different HPV types have been graded as high risk types (16 and 18) medium risk (30 and 33) and low risk (6 and 11). There is storng association with HPV sub types 6 and 11 for laryngeal papillomatosis and SCC arising in the pre-existent benign papillomas associated with same types. HPV 16, is more potent subtype associated with the verrucous sub type of SCC of the aero digestive tract. HE showed cancer and leukoplakia patients are older than controls and patients were to be chronic smokers or alcoholics. Study shows glottic SCCs show a higher human papilloma-high risk oncogene positivity than do the supraglottic SCCs and the hypopharynx shows the lowest positivity rate.

h. **Gastro– esophageal Reflux**: Laryngo pharyngeal reflex has received increasing attention as possible co – factor in laryngeal carcinogenesis.

Risk Factors for laryngeal Cancer

One hundred and seven patients afflicted with incident laryngeal cancer and 290 controls with diseases considered not related to tobacco and alcohol exposure were interviewed in the Universiy Hospital of Montevideo, Uruguay. The study showed that smoking to be a strong risk factor, with a risk ratio35 times that of non-smokers. Alcohol exposure displayed lesser effects but its interaction with tobacco smoking

resulted in very high risks (more than 100 times higher). Among particular types of alcoholic beverages, red wine showed risk ratios similar to those displayed by hard liquor consumtion. The habit of drinking a local tea called “mate” was associated with a threefold increase in risk, after controlling for the effects of age and tobacco and alcohol consumption. Infrequent consumption of vegetables and fruits showed risk ratio of on the order of 2.7, suggesting a role of diet in the causation of laryngeal cancer.

Multifactorial Theory of Squamous Cell Carcinogenesis

It is apparent that the risk factors may be inter connected, and that they may play complementary, even synergistic, roles in laryngel carcinogenesis. It is the distinct actions of these risk factors that fit a new multifactorial model of carcinogenesis in which mucosal inflammation, injury and / or infection play a critical role.

Classic carcinogenic theory relates to the dysregualtion of cellular growth and differentiation, carcinogenesis cause susceptible cells to undergo this dysregulation of growth and differentiation, which is termed malignancy. Initiation and promotion are the two recognized stages of carcinogenesis. Initiators are those carcinogens acting in the early phase of transformation; promoters act during the more variable late phase, within the latent time prior to malignant change.

Clinical observation suggest that HPV is exclusively an infection of squamous epithelium; it grows on skin, on squamous epithelial surfaces of aero digestive tract such as the nose and larynx, when it occurs in the tracheobronchial tree and lung, Squamous metaplatia of the normal epithelium is almost always found. Such metaplasia may be exacerbated by smoking, reflux or any other cause of chronic inflammation.

Whether HPV infection is a prerequisite for squamous carcinogenesis at all of the sites of its occurence remains to be seen.

Presently, tobacco is an important co-factor in laryngeal carcinogenesis, so too, preflex may be a very important co-factor. Ethanol appears to be greater risk factor, compared with tobacco; for the development of supraglottic squamous cell carcinoma. Because ethanol is not inhaled, it probable has little direct contact with the laryngeal mucosa. One might speculate that is exerts its effects by altering the immune status of the host, by predisposing to reflux or by both mechanisms.

In conclusion the relationship between HPV infection and environmental factors such as pollution, occupational exposures, tobacco smoke and reflux may yet prove to be profoundly interactive and Etiology and pathogenesis of laryngeal carcinoma may proved to be truly multifactorial.

EPIDEMIOLOGY

Total number of cases of carcinoma larynx in 2004 is 105 in our hospital

COMMON CANCERS (2002): CIR AND TREND (1982-2002)

IN MMTR, MALE

Common cancers in 2002	1982-1986	1987-1991	1992-1996	1997-2001	2002
Stomach	9.5	9.9	10.1	10.1	10.3
Lung	5.1	7.5	8.1	8.6	9.2
Oral caity*	5.0	5.7	5.8	6.1	7.6
Oesophagus	4.5	6.5	6.2	7.3	7.3
Lymphoma	3.8	4.3	4.1	4.7	5.8
Leukemia	2.6	2.6	3.4	3.5	4.9
Oropharynx*	3.3	4.6	4.4	4.8	4.7
Brain & CNS	1.9	2.0	2.5	2.7	3.8
Hypopharynx	3.1	4.1	4.0	4.2	3.4
Larynx	**2.8**	**3.2**	**3.2**	**3.9**	**3.2**

CIR: Crude Incidence Rate / 100.000
UICC Classification

Above table shows that carcinoma Larynx is among the top 10 cancers according to Madras Metropolitan Tumour Registry. Also the incidence is ever increasing.

PATHOLOGY & HISTOLOGY:

Laryngeal carcinoma constitutes approximately 2.5% of all head and neck malignancies. A slight increase in the incidence has been noted in the past two decades. 80% of laryngeal carcinoma occurs in the elderly in the fifth, sixth, seventh decades of life. A preponderance is noted in the males but this difference is decreasing because of increase in the number of female smokers. Post cricoid malignancy is seen more commonly in females than males.

The pathology of laryngeal cancer is very complex. It may be considered under the following headings:

Sites of incidence

Histological types

Histological grading

Spread of malignancy

Sites of incidence: Tumour incidence in different locations of the larynx varies. Most lesions occur in the glottic region followed by the supraglottis and subglottic regions in that order.

Glottic - 76%

Supraglottic - 19%

Subglottic - 5%

The laryngeal tumours may be

A. Epithelial

I. Squamous cell carcinoma – predominantly

II. Verrucous Carcinoma

III. Spindle cell carcinoma

Basaloid squamous cell carcinoma

B. Non epithelial

I. Adenoid cystic carcinoma

II. Neuro endocrine carcinoma

III. Malignant histiocytoma

IV. Osteo sarcoma

V. Rhabdomyo Sarcoma

VI. Fibro sarcoma

VII. Haemangio sarcoma

VIII. Malignant Schwanoma

IX. Chondro sarcoma

C. Lympho Proliferative Neoplasms

1. Extramedullary plasmocytoma
2. Lymphoma
3. Melanoma

D. Metastatic Lesions from

1. Renal cell carcinoma
2. Breast carcinoma
3. Melanoma

Histological types: Macroscopically, the growth could be exophytic, (proliferative), ulcerative or infiltrative. The most common type of tumour is the squamous cell carcinoma. Other rarer types of malignancy are:

Adeno Carcinoma	Malignant lymphoma
Adenoid Cystic Carcinoma	Fibrosarcoma
Chondrosarcoma	Plasmacytoma
Transitional cell Carcinoma	Malignant melanoma

Microscopically they are graded as, well differentiated, moderately differentiated and poorly differentiated by **Broder's** classification – Glottic tumours are usually very well differentiated.

Premalignant and early malignant laryngeal lesions:

Papillomas : They are well circumscribed, benign neoplasms of the lining squamous epithelium. There are two main varieties, juvenile and adult types. HPV virus is main etilogical factor. Juvenile papillomas are soft, Mobile, pale pink, lobulated and 2-5mm in diameter and multiple. Histologically, lesion consists of multiple, small, papillary processes, lined by thickned prickle cell layer without cellular atypia. Malignant transformation may be observed after irradiation. Adult papilloma is single, occurs in 2-3% of cases. HPV antigenic material was demonstrated in tissue sections of the tumours.

Keratosis : It is a form of hyperplasia of laryngeal epithelium They are often the outcome of chronic irritation. Histopathologically two forms of keratinisation are seen:- orthokeratosis – keratinized cells have shed their nuclei. Parakeratosis – the

Nuclei are pyknotic at the center of the cell. The incidence of carcinoma following keratosis is below five percent.

The descriptive terms, currently advocated by the W.H.O. are as follows

Hyperplasia

Keratosis

Mild dysplasia

Moderate dysplasia

Severe dysplasia

Carcinoma in situ

Crissman recommended a system analogous to that used in the uterine cervix for cervical intraepithelial neoplasia. This was termed laryngeal intraepithelial neoplasia (LIN).

LIN I : mild dysplasia and keratosis

LIN II : moderate dysplasia and intracellular dyskeratosis

LIN III : severe dysplasia and carcinoma in situ.

Carcinoma In situ and Carcinoma In situ with micro invasion

In Carcinoma in situ of larynx there is full thickness replacement of the epithelium by cells with malignant cytologic features but no invasion beyond basement membrane. Grossly one cannot differentiate from keratosis or keratosis with cell atypia (leukoplakia). If it is left, it may go for invasive carcinoma. The rate of larynx preservation was seven times higher than reported after radio therapy without local recurrence in these cases.

Squamous cell carcinoma

This is the most commonly encountered tumour in the larynx. The incidence is around 1% of all cancers. 2% of all cases of Head and neck cancer are squamous cell carcinoma. The male predominance is high. The age range varies form third to ninth decade. The peak incidence is seventh decade. The incidence is seventh decade. The incidence is much higher among urban dwellers than those reside in rural areas. To label a malignancy as squamous cell carcinoma certain distinguishing and specific futures of normal squamous epithelium must be present at the light microscopic level.

(i) Formation of Keratin – extra cellular or intra cellular

(ii) The presence of inter cellular 'bridges'

Verrucous Carcinoma (Ackerman's Tumour)

Exophytic, fungating, brodly, implanted with many heavy broad filiform projections, it is located in vocal cords. Microscopically thickened papillomatous folds covered with well-differentiated keratinizing squamous epithelium. Slowly growing and locally aggressive, clinically malignant. It does not spread by metastasis, destruction of the cartilage may be present. Treatment is surgical excision with complete removal of the tumour with adequate margin. Radiotherapy is contraindicated as it may change into anaplastic carcinoma.

Pseudo Sarcoma

Shows squamous cell carcinoma and sarcoma in the same region. Appearance is multiple polypoid lesion with ulcerated mucosa. Histalagical difference is present between primary and secondary sites

Basaloid Squamous cell carcinoma

Most frequently arises in supra glottis and hypopharynx. Prominent nuclei and scant cytoplasam and carries worse prognosis because of frequent distal metastases.

Histological Grading:

Degree of differentiation : The extent to which a squamous cell cancer retains the distinguishing features of normal stratified squamous epithelium determines the degree of differentiation. Accordingly Broder proposed a grading as well, moderate and poorly differentitated.

Well differentiated type: The individual tumour cell and nests show considerable similarity to normal stratified squmous epithelium. “Pearl” – a nest of cells some of that in whorled fashion with the central cells having more abundant eosinophilic cytoplasm than the peripheral cells and often showing central keratinization.

Moderately differentiated type : Considerable anaplasia is seen. Resemblance to normal stratified squamous epithelium is slight.

Poorly differentiated type: Considerable anaplasia is seen. Resemblance to normal stratified squamous epithelium is slight.

Grades	**% of Cell Undifferentiated**
Well Differentiated	0-25
Moderately differentiated	25-50
Poorly Differentiated	50-75
Undifferentiated	75-100

Spread of malignancy

Supraglottic Tumours : Aryepiglottic fold is the commonest site of involvement. Mostly exophytic tumours tend to remain localized for longer time. Supra glottic tumours are more apt to have pushing rather than invasive borders.

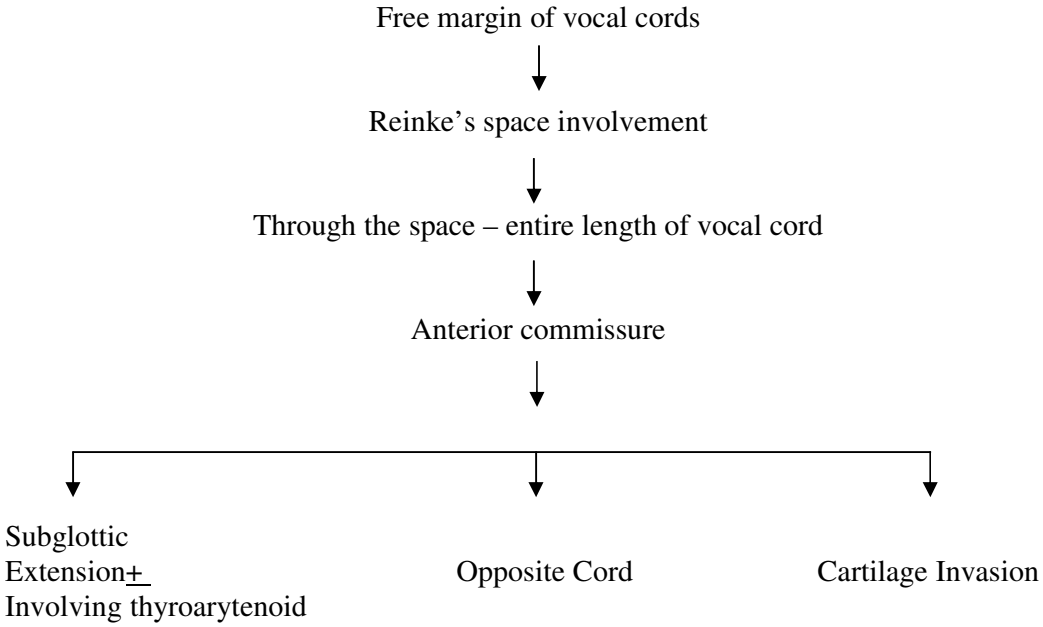
Mode of Spread

Superiorly	:	Submucosa of Vallecula
Anteriorly	:	Through holes in the epiglottic cartilage to the pre epiglottic space.
Inferiorly	:	False cords; through paraglottic space to true vocal cords and subglottic.

Malignant growth from false cords laterally go to pyriform fossa. Supraglottic tumours grow in the direction of the flow of submucosal lymphatics.

Glottic Tumours : in the glottis malignancy has a predilection for the anterior half of vocal cord and the anterior commissure.

Mode of Spread



Subglottic

Primary tumours of subglottic region are rare. They are mostly extensions from glottis and characterized by circumferential and infiltrating growth, cartilage invasion and penetration of cricothyriod membrane. Symptoms are airway obstruction.

Mode of Spread

Superiorly : Glottis

Anteriorly : Through cricothyroid membrane to grow outside the laryngeal framework

Inferiorly : Trachea

Trans Glottic Tumours: Tumours surrounding laryngeal ventricle (involving glottis and supraglottic regions). These are characterized by infiltrative growth pattern with frequent cartilage invasion and poor prognosis.

Barriers for spread of tumours: Pattern of growth and spread of laryngeal cancer are found to be influenced by fibro elastic ligaments and membranes.

1. Anterior commissure tendon
    a. Midline barrier for spread of glottic tumours
    b. It is the confluence of vocal ligament, thyroepiglottic ligament, conus elasticus and internal perichondrium of thyroid ala.
2. Conus elasticus – Barrier for spread to subglottic region

    quadrangular membrane forms barrier to supra glottis region.
3. Ventricles – Barrier for spread to supraglottis
4. Thyroid cartilage
5. Cricoid cartilage

Adenoid Cystic Carcinoma : Laryngeal adenoid cystic carcinoma (ACC) is rare and probably arises from endogenous seromucinous glands. Most laryngeal ACCs are either subglottic or supraglottic. Microscopically the tumour is characterized by tubular, cribriform and solid growth pattern. The solid growth pattern has wrose prognosis. ACC is infiltrative and has perineural invasion, which present with pain in patients. ACC commonly metastasis to lung and bone. Surgical excision with adjuvant radiotherapy is the treatment of choice.

Neuroendocrine Carcinomas: Three types of neuroendocrine carcinomas occur (i) typical carcinoid (well differentiated neuro endocrine carcinoma), (ii) atypical carcinoid (moderately differentiated neuro endocrine carcinoma), and (iii) small cell carcinoma (poorly differentiated neuro endocrine carcinoma).

Typical Carcinoid of the larynx is an extremely rare tumour with a strong male predominance. Microscopically it is characterized by islands, nests and ribbons of uniform small neoplastic cells lacking under nuclear atypia, mitotic figures or necrosis. Patients are usually treated by surgery.

Atypical Carcinoid is more common than typical carcinoid. Histologically these exhibit mild to moderate nuclear atypia, mitotic figures and single cell necrosis. They are immuno reactive for calcitonin, although the serum calcitonin level is rarely elevated. Forty percent of patients die with this disease. Surgery with or without adjuvant radiation and chemo therapy is the treatment of choice.

Small cell Carcinoma (Oat Cell Carcinoma) comprises 0.5% of primary laryngeal malignancies. The neoplastic cells are two or four times the size of a lymphocyte. Nucleus have a finely granular chromatin, lack of nucleoli and increased

fragility of the cells. It is associated with a dismal prognosis. Radiation and chemotherapy are the treatment of choice.

Chondrosarcoma is rare slowly growing cartilaginous tumour. It is the most common malignant measenchymal laryngeal neoplasm. These are typically submucosal and mostly arise from cricoid cartilage. It is firm in consistency, and is characterized by hyper cellularity, nuclear atypia and double nucleated cells. Surgery is the treatment of choice.

Lymphomas account for less than one percent of all laryngeal neoplasms. There is no significant difference in incidence between the sexes. The condition occurs from fifth to seventh decade. It involves the supra glottic region in particular the epiglottis and aryepiglottic folds, the vocal cords may be involved. Macroscopically the tumour appears as swelling covered by intact edematous mucosa. Microscopically most laryngeal lymphomas are of lymphocytic types Hodgkin's disease very rarely involves the larynx.

CLASSIFICATION AND STAGING:

Laryngeal tumours can be classified according to the region.

1. Supraglottic 18%
2. Glottis 76%
3. Subglottic 6%

TNM classification of carcinoma of larynx.

Rules for Classification

The classification applies only to carcinoma. There should be histological verification of the disease. Any unconfirmed cases must be reported separately. The minimum requirements for assessment are:

T (site)	:	Clinical examination, laryngoscopy and radiography
N (node)	:	Clinical examination
M (Metastasis)	:	Clinical examination and radiography

X indicates that the minimum requirements for assessment cannot be met.

Anatomical regions and sites

1. Supra Glottis

Epilarynx including Marginal Zone

i. Posterior surface of suprahyoid epiglottis (including the tip)

ii. Aryepiglottic fold

iii. Arytenoid

Supraglottic Excluding Epilarynx

iv. Infrahyoid epiglottis

v. Ventricular bands

vi. Ventricular cavities

2. **Glottis**

i. Vocal cords

ii. Anterior commissure

iii. Posterior commissure

3. **Sub Glottis**

Regional lymph nodes

The regional Lymphnodes are the cervical nodes.

TNM Pre Treatment Classification by UICC 1987

T. Primary Tumour

Supra Glottis

T_{is} Preinvasive carcinoma (carcinoma in situ)

T_0 No evidence of primary tumour

T_1 Tumour confined to the region with normal mobility of vocal cords.

T_{1a} Tumour confined to the laryngeal surface of epiglottis or to an aryepiglottic fold or to a ventricular cavity or to a ventricular band.

T_{1b} Tumour involving the epiglottis and extending to the ventricular cavities ir bands.

T_2 Tumour confined to the larynx with extension to adjacent site or sites or to the glottis without fixation.

T_3 Tumour confined to the larynx with fixation and/or other evidence of deep infiltration.

T_4 Tumour with direct extension beyond the larynx.

Glottis

T_{is} Preinvasive carcinoma (carcinoma in situ)

T_0 No evidence of primary tumour

T_1 Tumour confined to the region with normal mobility

T_{1a} Tumour confined to one cord

T_{1b} Tumour involving both cords

T_2 Tumour confined to the larynx with extension to either the supraglottis or the subglottic regions with normal or impaired mobility.

T_3 Tumour confined to the larynx with fixation of one or both cords

T_4 Tumour with direct extension beyond the larynx or thyroid cartilage invasion.

Sub Glottis

T_{is} Preinvasive carcinoma (carcinoma in situ)

T_0 No evidence of primary tumour

T_1 Tumour confined to the region

T_{1a} Tumour confined to one side of the region

T_{1b} Tumour with extension to both sides of the region

T_2 Tumour confined to the larynx with extension to one/or both cords with normal or impaired mobility.

T_3 Tumour confined to the larynx with fixation of one or both cords

T_4 Tumour with destruction of cartilage and /or with direct extension beyond the larynx.

N- Regional lymph Nodes

N_x Regional lymph nodes cannot be assessed

N_0 No regional lymph node metastasis

N_1 Metastasis in a single ipsilateral lymph node 3 cm or less in greatest dimension.

N_2 Metastasis in a single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension, or in multiple ipsilateral lymphnodes none more than 6 cm in greatest dimension, or in bilateral or contralateral lymph nodes none more than 6 cm in greatest dimension.

N_{2a} Metastasis in a single ipsilateral lymphnode more than 3cm but none more than 6cm in greatest dimension.

N_{2b} Metastasis in multiple ipsilateral lymphnode none more than 6cm in greatest dimension.

N_{2c} Metastasis in bilateral or contralateral lymph node none more than 6 cm.

N_3 Metastasis in a lymphnode more than 6cm in greatest dimension.

M- Distant Metastasis

M_0 No evidence of distant metastasis

M_1 Evidence of distant metastasis

M_x The minimum requirements to assess the presence of distant metastasis cannot be met.

STAGING

Stage I	**T_1**	**N_0**	**M_0**
Stage II	T_2	N_0	M_0
Stage III	T_1 / T_2 / T_3	N_1	M_0
	T_3	N_0	M_0
Stage IV A	T_4	N_0	M_0
Stage IV B	Any T	N_2 / N_3	M_0
Stage IV C	Any T	Any N	M_1

Differential diagnosis:

1. Fungal laryngitis,
2. TB larynx,
3. sarcodosis,
4. wegeners granulomatosis.

Investigation:

1. Routine Blood examination
2. X- ray chest – To look for secondaries and for GA fitness
3. X-ray Neck soft tissue lat view – To look for sub glottic air column and any widening of prevertebral soft tissue.
4. Ultrasound Neck – Thyroid gland involvement and neck secondaries.
5. Ultrasound Abdomen – To look for secondary deposits in liver.
6. CT Scan Neck – To see Pre epiglottic space, para glottic space, cartilage invasion.
7. Direct laryngoscopy – To know the extent of disease and biopsy
8. Barium swallow

CT Criteria for positive nodes:

- More than 1 cm diameter
- Spherical
- Peripheral rim enhancement with contrast and central necrosis.
- Extra capsular spread

Management Protocol:

1. **For carcinoma in situ**: When lesions clearly show hyperkeratosis with atypia and often CIS, management can be conservative if a satisfactory strip of cord is removed. The gross lesion should be removed, requiring frequent follow-up and rebiopsy 6 to 12 weeks later if needed.
2. **For T_1 and T_2 lesion** – Radiotherapy is the Ist choice of treatment
3. **For T_3 lesions** – Total laryngectomy with or without primary TEP
4. **For T_4 lesions** - Salvage Surgery

Post operative radiotherapy for T_3 and T_4 cases with or without nodal secondaries. For cases with advanced disease like stage IV, palliative radiotherapy with chemotherapy is given. Also cases who are not fit medically, are given RT. Involvement of Thyroid cartilage is contra indication for RT.

Local cure by radiotherapy for glottic tumors, which most always matches tumor-free survival, has not changed since 1974 when Fletcher and Jesse noted 85% control rate until 1996 when McLaughlin and others noted 89%. Surgical management of radiation failures resulted in a 60% salvage rate with a 70% salvage rate reported by Biller and Lawson and a 95% salvage rate reported by Rothfield and others. The latter result is achieved when partial surgery can be performed despite radiation failure.

No clear advantage of surgery versus radiotherapy is noted in the literature for early glottic tumor, and local mores and abilities should prevail. Surgery is more successful for lesions with subglottic extension and impaired vocal mobility.

Postradiation edema for longer than 6 months has a 45% association with deeply invasive recurrence and requires follow-up by endoscopy and imaging.

Post operative radiation is advised for cartilage destruction, subglottic extension, thyroid gland involvement or positive paratracheal nodes.

Prognotic Factors

Tumor Factor: Tumor Grade:

Poorly differentiated tumors carries worse prognosis.

It responds well to RT, but recurs.

Tumor Border:

Infiltrating border carries worse prognosis than pushing border

Surgical Margin:

Tumor free margin confirmed by frozen section carries better prognosis.

Lymph node status:

Number, location, Extra Capsular Spread are important criteria.

Among these Extra Capsular Spread is the single most important criteria.

Host Factor:

The type and degree of the host inflammatory response to tumor may bear on prognosis. Pronounced tumor- associated tissue eosinophilia (TATE), peritumoral Langerhans cell infiltration, and marked lymphoid inflammation have been touted as indicators of a good prognosis. Recently, however, the prognostic significance of TATE in LSCC has been disputed.

It is obvious that earlier the patient seeks medical advice, better is the prognosis.

PROFORMA OF THE CASE SHEET

Study Serial No.	OP.No.	Unit	IP No.	Date of First Visit

Follow up Dates	1	2	3	4	5	6	7	8

Name : Age : Sex :

Occupation : Income: Address:

Diagnosis :

I. Presenting Complaints

Hoarseness of voice, Difficulty in breathing, Cough, Difficulty in swallowing, Pain, Fever, Swelling in the neck, Loss of weight, Any other complaints:

II. History of Presenting Illness

Hoarseness of voice, Difficulty in breathing, Cough, Difficulty in swallowing, Pain, Fever, Swelling in the neck, Loss of weight, Associated complaints:

III. Past History

- History of Tuberculosis / Syphilis / Leprosy / diabetes
- History of trauma / allergy / irridation

Surgery for any other disease.

IV. Family History

- Similar complaints in any other member in the family

- Death related with cancer in the family.

IV. Personal History

- Habits: Smoking, Paan / Beet at nut chewing, Alcohol intake

V. Treatment History

VII. General Examination

Built, Nutrition, Mental Status, Pallor, Lymph – node status

Temperature, Pulse, Respiratory rate, Blood Pressure

VIII. Systemic Examination

Cardiovascular system, Respiratory system,

Per Abdomen, Central Nervous systems

IX. ENT Examination / Local Examination

1. Mouth : Lips, Teeth, Gum Margin, Palate, Floor of mouth

Pillars, Tonsils, Uvula, Posterior pharyngeal wall, Nasopharynx:

Throat : Indirect Laryngoscopy:- Posterior 1/3 of tongue, Vallecula,

Epiglottis, Aryepiglottic Fold, Arytenoids, Ventriculars bands,

vocal cords, Anterior & Posterior commissure, Pyriform fossae and

Postcricoid region, External palpation of laryngeal cartilages

Examination of Neck

2. Nose :

3. Ear :

X. Provisional Diagnosis

XI. Investigations

a. X-ray Chest / Barium Swallow / X-ray Neck – Lateral view (soft tissue)

b. Biopsy – during DL Scopy & HPE / USG / CT - Neck

c. MLE & Biopsy for vocal cord lesion

d. FNAC of Neck nodes.

XII. Diagnosis

XIII. Management

XIIII. Follow Up

Meterial and Methods

This is an analytical, prospective, cross sectional study. An average of 400 cases attend the out patient department of our institute, Madras Medical College and Govrnment General Hospital, Chennai, daily. Of these 3 to 4 patients harbour malignancy of various sites in the head and neck region.

Fifty consecutive cases with proven laryngeal malignancy who were admitted in ENT ward of this hospital were taken up for the study.

Inclusion Criteria:-

Only Histologicaly proven cases of ca larynx are taken up for study.

Exclusion Criteria:-

Patients with laryngo pharyngeal malignancy are excluded.

Evaluation of the disease is done by history, Clinical Examination using Indirect laryngoscopy. Neck examination, ultra sound or CT of neck, video laryngoscopy, Direct laryngoscopy & Biopsy for supra glottic lesion, Micro laryngial examination & biopsy for vocal cord lesion, FNAC for neck nodes. Most often radiological examination of neck up stages the disease. Endoscopy is used to visualise areas like laryngeal surface of epiglottis and anterior Commisures, which are usually hidden areas.

OBSERVATION AND DISCUSSIONS

Site, Morphology & Staging:

The majority of the cases were Glottic carcinoma 60%. Supraglottic constitute 32% and rest of the cases are Transglottic 6% and subglottic 2%. This study concurs with the standard literature.

Twenty eight patients had Proliferative fleshy lesions, another five cases were found to have UIcero proliferative lesions. Twelve cases had smooth mucosal surface.

As shown in the standard literature the carcinoma of the glottic region dominate in our study. Majority of the cases presented at T_3 stage especially glottic carcinoma.

Incidence by Site, T – stage and Nodel status (N=50)

Anatomical Site	Stage	No. of cases	%	N Stage	No.of Cases	%
Supraglottic 16- cases	T_1	-	-	N_0	0	0
	T_2	4	25	N_1	4	25
	T_3	9	56.25	N_2	8	50
	T_4	3	18.75	N_3	4	25
Glottic 30- cases	T_1	8	26.7	N_0	21	70
	T_2	2	6.7	N_1	8	26.7
	T_3	18	60	N_2	1	3.3
	T_4	2	6.7	N_3	-	-
Trans glottic 3- cases	T_1	-	-	N_0	-	-
	T_2	-	-	N_1	1	33.3
	T_3	3	100	N_2	2	66.6
	T_4	-	-	N_3	-	-
Sub glottic 1- case	T_4	1	100	N_2	1	100

Discussion on the table

i. 60% of the cases are glottic cancers. It is regrettable that majority of patients (18 cases) reached hospital when they reach T_3 stage. 10 cases were in the T_1 & T_2 stages. Two patient presented in the T_4 stage. Majority of glottis cancers patients (21) presented with No, eight cases the N_1 and one in N_2 stage. None presented with metastasis.

ii. 32% are supraglottic cancers. 75 percent presented in T_3, T_4 stage only 25% presented in T_2 stage. None came on T_1 stage. None of the cases presented in N_0 stage. 50% presented in N_2 stage. This shows that supra glottis cancers have the predilection of nodal metastases.

iii. All the trans glottic cases presented with Neck secondaries in N_1 or N_2 stage.

iv. Only one case of sub glottic cancer found.

Stage of the diseases when presented is crucial in deciding the type of treatment to be given.

HISTOLOGICAL FINDINGS IN THIS STUDY

Broder's classification when applied in our study the following pattern is observed.

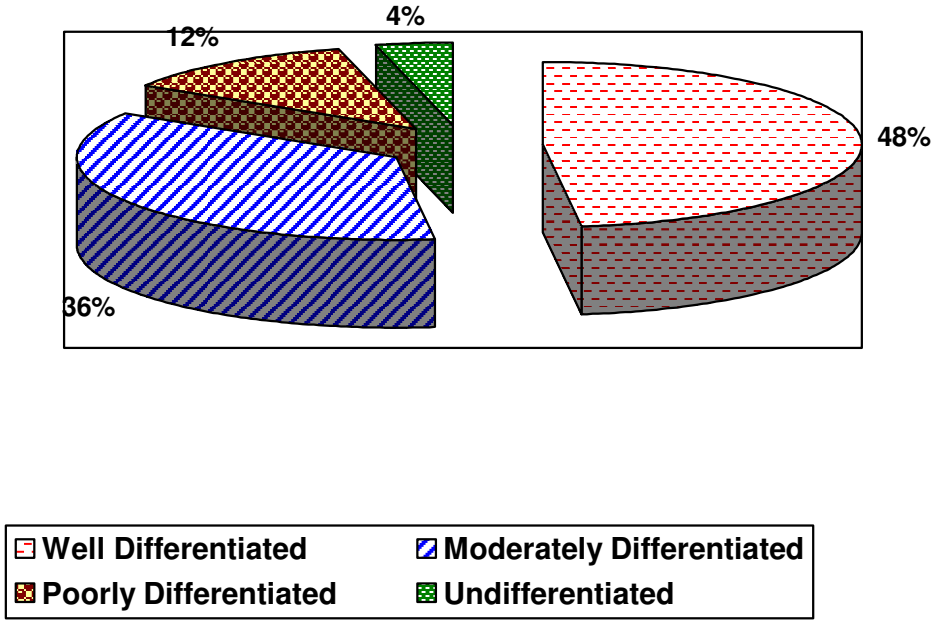
Differentiation	**No.of Cases**	**Percentage**
Well differentiated	24 cases	48%
Moderately differentiated	18 cases	36%
Poorly differentiated	6 cases	12%
Undifferentiated	2	4%

Since majority of the cases where glottic growth which have the tendency to present as well differentiated variety, as shown in the standard literature. In our study predominately more well differentiated variety (48%) is seen.

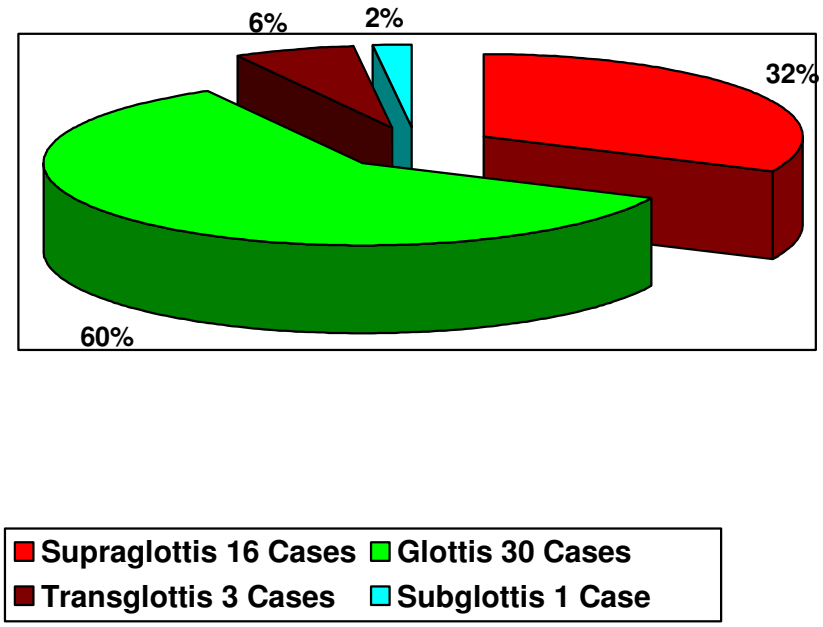
ANATOMICAL SITE OF LESION AND DIFFERENTIATION WITH PERCENTAGE

	Anatomical Site No.of cases	**Differentiation**	**Percentage**
1.	Supraglottis 16 cases	Well differentiated - 4 Moderately differentiated - 4 Poorly differentiated - 2 Un- differentiated - 2	25% 25% 12.5% 12.5%
2.	Glottis 30 cases	Well differentiated - 20 Moderately differentiated - 10 Poorly differentiated - Nil	66.7% 33.3% Nil
3.	Transglottis 3 cases	Well differentiated - Nil Moderately differentiated - 3 Poorly differentiated - Nil	Nil 100% Nil
4.	Subglottis 1 case	Moderately differentiated - 1	100%

DISTRIBUTION ACCORDING TO DEGREE OF DIFFERENTIATION



DISTRIBUTION ACCORDING TO ANATOMICAL SITE



Supra glottic (25%) and glottic tumour (66.7%) are well differentiated variety. All the transglottic tumours were (100%) moderately differentiated. Cells nests are observed in 46 cases out of 50 cases (92%0 Inflammatory cell infiltration in the stroma are seen in all the cases. Predominantly neutrophils with macrophages and plasma cells seen in 26 cases 52%. These cases had presented with symptoms less than 6 to 9 months. This may be due to acute tumour cell reactions. The other 24 cases had lymphocytes (48%) along with plasma and macrophages. This indicates chronic process initiating host response. These cases may have better prognosis.

Type of Inflammatory Cell	**No.of Cases**
Sinus histiocytosis, follicular lymphoid hyperplasia, plasma cells	33
Lymphoid depletion	5

Sinus histiocytosis, follicular lymphoid hyperplasia, plasma cells are associated with good prognosis.

Lymphoid depletion is associated with poor prognosis.

Conventional Squamous Cell Carcinoma

Among the conventional squamous cell carcinoma 48% were well differentiated and 32% were moderately differentiated. Poorly differentiated is variety observed in two cases. These cases are presented with node involvement initially. Histologically it reveals elongated and fusiform neoplastic cells. The mitotic figures are more. The cells are highly pleomorphic and based on the morphological features it is classified as poorly differentiated squamous cell carcinoma. These patients are subjected to palliative radiotherapy.

Mitotic Figures in our Study

Mitotic Figures	No. of Cases	%
Scanty	42	84
Moderate	4	8
High	4	8

In undifferentiated carcinoma histological examination reveals sheets of neoplastic cells with hyperchromatic pleomorphic nuclei and eosinophilic cytoplasm is observed. Moderate amount of fibrovascular tissue surrounded with neoplastic cells. Scattered infiltration with mononuclear cells is observed in the stromal tissues. The treatment rendered is radiotherapy.

TREATMENT ADOPTED IN OUR STUDY

Since Organ Preservation is the main aim nearly 50% of the cases are subjected to Curative Radiotherapy when they present with T1, or T2 stage without metastases.

In our study, out of 50 cases Curative radiotherapy is given for 22 cases who presented in early stage of the disease. Palliative radiotherapy with Chemotherapy given for 10 cases who presented with late stage of the disease. 13 patients underwent Total Laryngectomy, out of which 12 patients were in the stage III and one in Stage IV. Ideally, most cases are glottic cancers with T3 stage without nodal or distant metastases. Two cases underwent modified radical neck dissection along with Laryngectomy.

Five cases absconded from treatment. There are eight cases of recurrence within the period of 2 years. Out of which one case was after Total Laryngectomy with modified radical neck dissection. That case was not subjected to post operative radiotherapy since that patient developed post operative Pharyngo cutaneous fistula and Subsequently he underwent myocutaneous flap transposition procedure. So we are unable to give Radiotherapy within about 4 months.

Two cases of recurrence occured after primary Radiotherapy for Glottic cancer T1 No Mo and T3 No Mo. Those patients underwent total Laryngectomy who is disease free till now. Post radiation oedema of more than 6 months was

considered as the criteria for surgery in first case. Residual lesion was considered as the criteria for surgery for second case.

Remaining cases were given adjuvant Chemotherapy with Palliative procedures. All the recurrent cases were presented with nodal metastasaes initially. Histologically lymphoid depleted cases of 5 went in for recurrence. All the poorly differentiated cases responded well to Radiotherapy.

Tumour Grade is not predicted as the important prognostic indicator as many literature studies shows

Adequate resection of tumour, leaving tumour free margin resulted in disease free survival till 2 years – Literature also concurs with this.

CONCLUSION

- Primary Radiotheraphy given : 22 Cases
- Surgery and Post Operative : 11 Cases
  Radio Theraphy
- Surgery done for Radio : 2 Cases
  Recurrent Cases
- Total No. of Recurrences : 8 Cases
  within the period of 2 years
- 2 Years Survival Rate : 82 %
  after curative RT and Surgery

BIBLIOGRAPHY

1. Alfio Ferlito, and Gianfranco Recher: Ackerman's Tumour (Verrucous Carcinoma) of the Larynx Cancer 46: 167-1630, 1980.

2. Amendola BE, Amendola MA, McClatchey KD: Radiation induced carcinoma of the larynx, Surg Gynecol Obset 161: 30-32, 1985.

3. Arends MJ Wyllie AH, Bird CC: Papilloma viruses and human cancer Human Pathology 21:686-698, 1990.

4. Batsakis JG, E1-Naggar AK, Luna MA: Neuroendocrine tumours of larynx, Ann Otol Rhinol Laryngol – 101: 710, 1992.

5. Broders A.C. practival points on the microscopic grading of carcinoma New York State Journal of Medicine 32, 667-671 (1932).

6. Crissman J.D. laryngeal keratosis preceding laryngeal carcinoma. Archives of otolaryngology 108. 445-448: (1982).

7. Daham D., Sessions G., Peniello C, "Primary subglottic cancer", Laryngoscope 108, 741-745, 1998.

8. Doyde DJ, Henderson LA, Lejeune FE: changes in human papilloma viruses typing of recurrent respiratory Papillomatosis progressing to malignant neoplasm. Arch Otolaryngol Head Neck Surg 120: 1273-1276, 1994.

9. Damm N, Sittel C, Streppel M, Eckel He, Transoral C02 laser for surgical management of glottic carcinoma in situ. Laryngoscope 110 (7): 1215-21, 2000.

10. DeStefani, E, Correa P, Oreggia F, Risk factors for laryngeal cancer. Cancer 60: 3087-3091, 1987.

11. Eduardo De Stefani, Pelayo correa, Fernando Oreggia, Juan Leiva, Santiago Rivero, Gustavo Fernandez, Hugo Deneo – pellegrini, Diego Zavala, and Elizabeth Fontham : Risk factors for Laryngeal cancer Cancer: 60: 3087-3091, 1987.

12. Filipowski M. Kurnicki W, Sieskiewixa A, Management of lymph node metastases in larynx surgery with organ preservation: Otolaryngologia Polska, 54, 31: 140-1, 2000.

13. Graham S, Mettlin C, Marshall J. : Dietary factors in the edipemiology of cancer of larynx. Am.J. edidemiology. 113: 675-680, 1981.

14. Groome PA. O' Sullivan B. Irish JC, Rothwell DM, Math KS, Bissett RJ, Dixon PR, Eapen LJ, Gulavita SP, Hammond HA, Hodson DI, Mackenzie RG, Schneider KM, Warde PR, Mackillop WJ: Glottic cancer in Ontario, Canada and the SEER areas of the Unites States. Do different management philosophies produce different outcome profiles? Journal of Clinical Epidemiology. 54(3): 301-15, 2001.

15. Guenel P Chastang J-F, Luce D. A study of the interaction of alcohol drinking and tobacco smoking among French cases of laryngeal cancer J. Epidemiol common health 42: 350-354, 1988.

16. Hausfeld J.N.; "Hoarseness current concept on etiologies and treatment alternatives", Med J.: 47 (2); 59-63, 1998.

17. Hermanet P. and Sobin, L.H, UICC TNM classification of malignant tumours 4th edition 1987.

18. International Union Against Cancer (UICC) Report on the prevalence of malignancies world wide – 2002.

19. Jacques Pinsolle, Vincent Pinsolle, Claire Majoufre, Stephane Duroux, Helene Demeaux, Francois Siberchicot. Prognostic Value of Histologic findings in Neck Dissections for Squamous Cell Carcinoma. Arch otolaryngol head neck surgn / 123, 1997.

20. James A. Koufman, Alan J. Burke – The etiology and pathogenesis of laryngeal carcinoma, current concept in laryngeal cancer I.30: 1-19, 1997.

21. James O, Cappellari, M.D., Histopathology and pathologic prognostic indicators of laryngeal cancer, Oto laryngologic clinics of North America, 30: 251-268, 1997.

22. James A. Koufman, Alan J. Burke – The Oto-Laryngology Clinic's of North America – The Etiology and Pathogenesis of Laryngeal Carcinoma Laryngeal Cancer I. 1-19, 2000.

23. Koufman JA: The otolaryngologic manifestations of gastroesophageal reflux disease. Laryngoscope 101 (suppl 53): 1-78, 1991.

24. Lindberg R. Distributions of cervical lymphnodes metastases from squamous cell carcinoma of the upper respiratory and digestive tracts cancer 29: 1146-149, 1991.

25. Mantra Vadi RVP, Liebner EJ, Haas re et.al cancer of glottis, prognostic factors in radiation therapy. Radiology 149: 311-314, 1983.

26. Olofsson J. Van Nostrand AWP: Adenoid cystic carcinoma of the larynx. A report of four cases and a review of the literature. Cancer 40: 1307, 1997.

27. Pollan M, Lopaz – Abenete G: Wood- related occupations and laryngeal cancer. Cancer detect prev. 19:250-257, 1995.

28. Ramadan M.F., Morton R.P – "Review: epidemiology of laryngeal cancer". Clinical otolaryngology 1.7: 417-428, 1982.

29. Report of the Population Based Cancer, Registry (PBCR) – of Chennai Region (ICMR) – 2002.

30. Silver Carl E., - "Historical aspects" In Silver's "Surgery for cancer of the larynx and related structures", Newyork Churchill living stone, 1.10:13-23, 1981.

31. Stephen H. Bennett, James W, Futrell, Joel A.Roth, Robert G. Hoye, and Alfred S. Ketcham, Prognostic significance of histologic host response in cancer of the larynx or hypopharynx Cancer: 28, 1996.

32. Wax MK, Touma BJ, Management of the No neck during salvage Laryngectomy: Laryngoscope 109 (1) 4-7, 1999.

33. Weir Neil, "Anatomy of the larynx and trachaebronchial tree". In Gleeson Michael – Scott- Brown's Basic Science Vol-1, 6th edition, London; Butterworth – Heinemann – 1/12/1-1/12/28,1/4/1-1/14/27, 1997.

34. Freeman DE, Mancuso AA, Parsons JT, et al: Irradiation alone for supraglottic larynxcarcinoma: Can CT Findings predict treatment results? Int J Radiat Oncol Biol Phys 19:485-490. 1990

35. Huang DT, Johnson CR, Schmidt-Ullrich R. Grimes M: Postoperative radiotheraphy in head and neck carcinoma with extracapsular Iymph node extension and/or positive resection margins. A comparative study. Int. J. Radiat Oncol Biol Phys 23: 737-742, 1992.

36. Kaplan El., Meier P: Nonparametric estimation from incomplete observations. Journal of the American Statistical Association 53:457-841, 1958.

37. Lee NK, Goepfert H. Wendt CD: Supraglottic laryngectomy for intermediate-stage cancer: U.T.M.D. Anderson Cancer Center expeerience with combinied therapy. Laryngoscope 100:831-836, 1990.

38. Lutz CK, Johnson JT, Wagner RL., Myers EN: Supraglottic Carcinoma: Patterns of recurrence, Ann Otol Rhinol Laryngol 9:12-17, 1990

39. Mendenhall WM, Million RR, Elective neck irradication for squamous cell carcinoma of the head and neck Analysis of time-dose factors and causes of failure. Int. J. Radiat Oncol Biol Phys 12-741-746, 1986.

40. Mendenhall WM, Million RR, Bova FJ: Analysis of time-dose factors in clinically positive neck nodes treated with irradiation alone in squamous

cell carcinoma of the head and neck, Int. J. Radiat Oncol Biol Phys 10-639-643, 1984

41. Mendenhall WM, Million RR, Cassisi NJ: squamous-cell carcinoma of the head and neck. Head neck Surg 3:15-20, 1980.

42. Mendenhall WM, Million RR, Cassisi NJ: squamous-cell carcinoma of the supraglottic larynx treated with radical irrdiation: Analysis of treatment parameters and results. Int. J. Radiat Oncol Biol Phys 10-2223-2230,1984

43. Mendenhall WM, Million RR, Cassisi NJ: squamous-cell carcinoma of the head and neck treated with radiation theraphy: The role of neck dissection for clinically positive neck nodes, Int. J. Radiat Oncol Biol Phys 12:733-740, 1986.

44. Mendenhall WM, Persons JT, Stringer SP, et al: Stage T3 squamous cell carcinoma of the glottic larynx: A comparison of laryngectomy and irradiation. Int. J. Radiat Oncol Biol Phys 23:732, 1992

45. Mendenhall WM, Persons JT, Stringer SP, et al: Carcinoma of the supraglottic larynx: A basis for comparing the results of radiotherapy and surgery. Head Neck 12: 204-204-209, 1990

46. Parsons JT, Mendenhal WM, Stringer SP, et al: Salvage surgery following radiation failure in Squamous cell carcinoma of the supraglottic larynx. Int. J Radiat Oncol Biol Phys 32-605-609, 1995

47. Pfister DG, Strong E, Harrison L., et t: Larynx Preservation with combined chemotheraphy and radiation therapy in advanced but resectable head and neck cancer. J. Clin Oncol 9:850-859, 1991

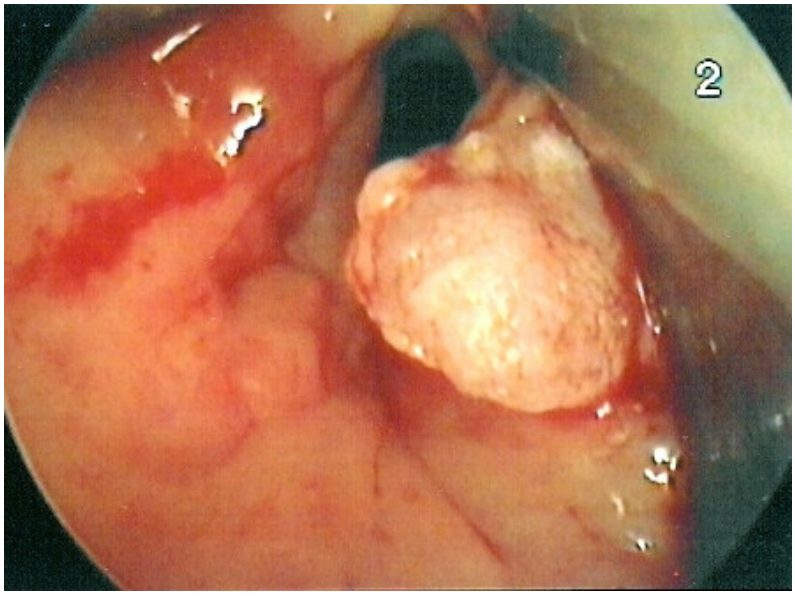
48. Stell PM: Adjuvant chemotherapy in head and neck cancer, Semin Radiat Oncol 2:195-205, 1992.

49. The Department of Veterans Affirms Laryngeal Cancer Study Group: Induction chemotherapy plus radiation compared with surgery plus radiation in patients with advanced laryngeal cancer N.Engl. J.Med 324:1685-1690,1991

50. Wang Z-H, Million RR, Mendenhall WM, et al: Treatment with preoperative irradiation and surgery of squamous cell carinoma of the head and neck. Cancer 64-32-38, 1989

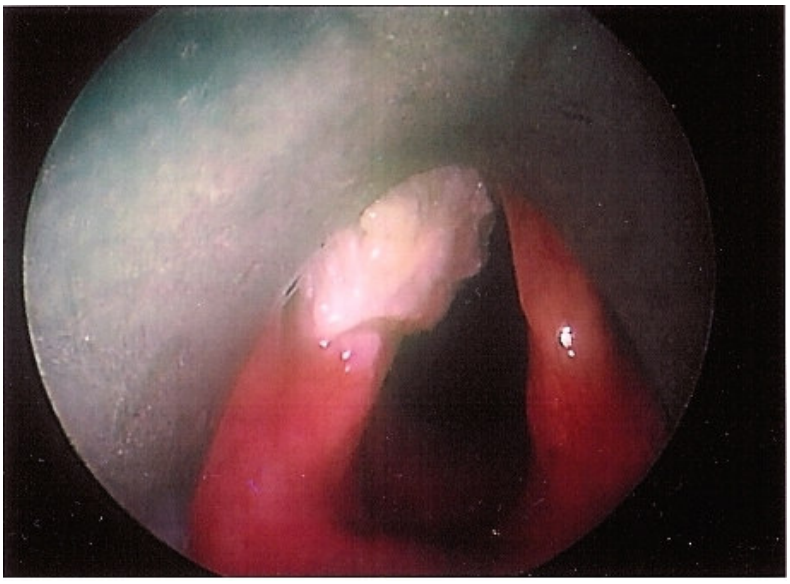
CARCINOMA SUPRAGLOTTIS

STAGE - III



CARCINOMA GLOTTIS

STAGE - III



CARCINOMA SUB GLOTTIS

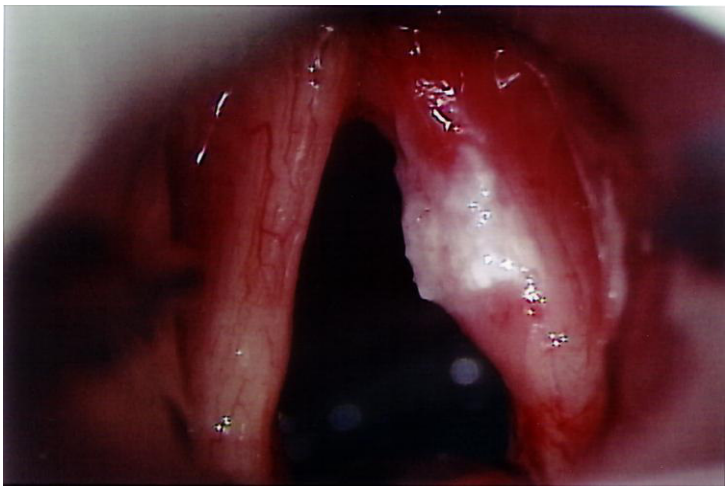
STAGE – IV

CASINOMA SUPRA GLOTTIS

POST RADIATION OEDEMA AFTER 6 MONTHS

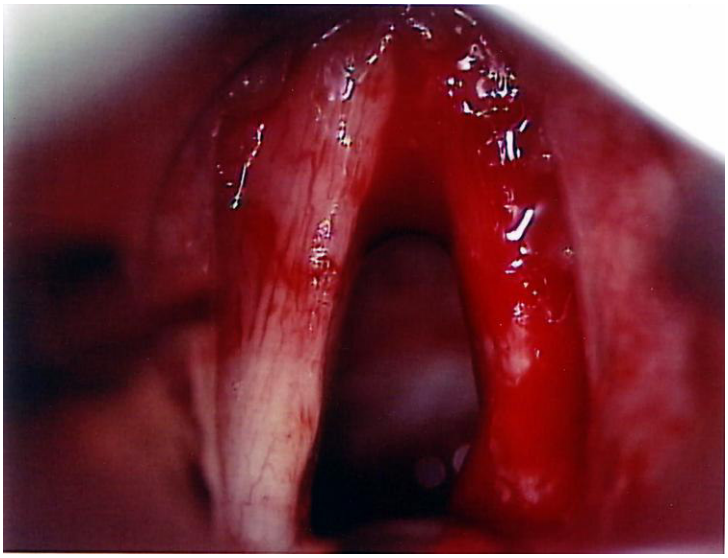
GLOTTIC CARCINOMA

STAGE - I



GLOTTIC CARCINOMA

POST IRRADIATION

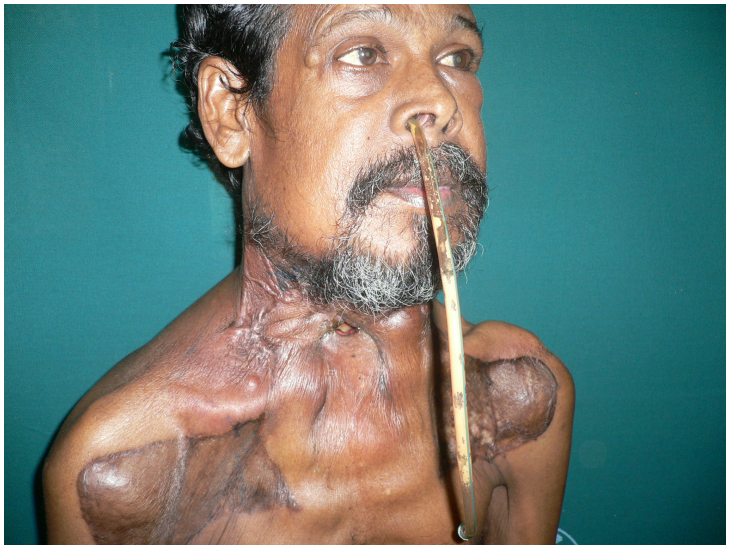


GLOTTIC CARCINOMA

POST LARYNGECTOMY WITH HEALTHY STOMA

GLOTTIC CARCINOMA

POST LARYNGECTOMY WITH NODAL RECURRENCE



S.No.	Name	Age	Sex	Staging	Treatment given
1.	Kamalam	62	F	T3 No. Mo	Curative Radiotheraphy
2.	Ravi	47	M	T3 N2b Mo	Palliative Radiotheraphy
3.	Damotharan	75	M	T2 No Mo	Curative Radiotheraphy
4.	Rangarajan	55	M	T3 N2b Mo	Palliative Radiotheraphy
5.	Rajeswari	30	F	T1 No Mo	Curative Radiotheraphy
6.	Elumalai	55	M	T3 N2b Mo	Total Laryngectomy with Neck Dissection with RT
7.	Balavantha Rao	65	M	T3 No Mo	Curative Radiotheraphy
8.	Dhanabal	55	M	T3 No Mo	Total Laryngectomy with RT
9.	Krishnaiah	75	M	T4 No Mo	Palliative RT with Chemotheraphy
10.	Ragavaiah	55	M	T3 No Mo	Absconded
11.	Abdul Rahman	70	M	T2 No Mo	Curative Radiotheraphy
12.	Vijayaraghavan	60	M	T4 No Mo	Palliative Radiotheraphy
13.	Manikandan	22	M	T3 No Mo	Curative Radiotheraphy

14.	Kannan	55	M	T1 No Mo	Curative Radiotheraphy
15.	Krishnan	69	M	T3 No Mo	Curative Radiotheraphy
16.	Dawood	65	M	T3 No Mo	Total Laryngectomy with RT
17.	Mohan	54	M	T4 No Mo	Total Laryngectomy with RT
18.	Murugan	34	M	T3 N1 Mo	Curative Radiotheraphy
19.	Poongavanam	56	M	T2 No Mo	Curative Radiotheraphy
20.	Kuttiappan	68	M	T2 No Mo	Curative Radiotheraphy
21.	Fathima	70	F	T3 No Mo	Palliative Radiotheraphy
22.	Jayalakshmi	70	F	T3 No Mo	Total Laryngectomy with RT
23.	Poongavanam	50	M	T3 No Mo	Total Laryngectomy with RT
24.	Chinnappan	55	M	T4 N3 Mo	Palliative Radiotheraphy with Chemotheraphy
25.	Prakash	40	M	T3 N3 Mo	Palliative Radiotheraphy with Chemotheraphy
26.	Nagendran	45	M	T3 N1 Mo	Curative Radiotheraphy

27.	Venkateshwaralu	29	M	T1a No Mo	Curative Radiotheraphy
28.	Rajendran	40	M	T1a No Mo	Curative Radiotheraphy
29.	Munusamy	70	M	T2 N1 Mo	Curative Radiotheraphy
30.	Gopal	65	M	T3 N2a Mo	Total Laryngectomy with RT
31.	James	55	M	T3 N1 Mo	Curative Radiotheraphy
32.	Jagadesan	85	M	T1a No Mo	Absconded
33.	Antony	50	M	T1a No Mo	Curative Radiotheraphy
34.	Sundaram	75	M	T4 No Mo	Palliative Radiotheraphy with Chemotheraphy
35.	Rajendran	57	M	T3 N1 Mo	Curative Radiotheraphy
36.	Chinnasamy	65	M	T3 N1 Mo	Curative Radiotheraphy
37.	Selvaraj	52	M	T3 N3 Mo	Absconded
38.	Chelliah	65	M	T4 No Mo	Total Laryngectomy with RT
39.	Kannan	63	M	T3 N2c Mo	Curative Radiotheraphy
40.	Samboornammal	64	F	T4 N2b Mo	Palliative Radiotheraphy with Chemotherapy

41.	Kesavan	57	M	T3 N1 Mo	Curative Radiotheraphy
42.	Munusamy	57	M	T3 N2c Mo	Absconded
43.	Rami Reddy	55	F	T3 No Mo	Curative Radiotheraphy with Total Laryngectomy
44.	Shantha Kumar	62	M	T4 N2b Mo	Palliative Radiotheraphy with Chemotheraphy
45.	Sivakumar	55	M	T1a No Mo	Curative Radiotheraphy with total Laryngectomy
46.	Mani	57	M	T3 N2a Mo	Total Laryngectomy with MRND
47.	Mohd. Ali	55	M	T3 No Mo	Total Laryngectomy with RT
48.	Kasi	50	M	T2 N1 Mo	Curative Radiotheraphy
49.	Moorthy	48	M	T3 No Mo	Total Laryngectomy with RT
50.	Shanmugam	88	M	T3 N3 Mo	Palliative Radiotheraphy with Chemotheraphy